CLAIMS

1. A method for the preparation of human, humanized or chimæric antibodies or polypeptides comprising Fc region of human IgG, said antibodies or polypeptides having different binding profiles, wherein said method comprises the steps consisting of :

a) providing candidate human, humanized or chimæric antibodies or polypeptides comprising Fc region of human IgG produced naturally by or following transfection with a vector comprising the coding sequence for said antibody or polypeptide of cells from animal cell lines comprising hybridoma, heterohybridoma, EBV-transformed human B cell lines or from eukaryotic microorganisms,

b) testing the binding of said antibodies or polypeptides on Fcgamma receptors including FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB,

c) selecting antibodies or polypeptides which :

i) bind to both FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB, or

ii) bind to both FcgammaRIIA and FcgammaRIIB but do not bind or bind only weakly to FcgammaRIIIA, or

iii) do not bind or bind only weakly to both FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB.

2. A method according to claim 1, wherein said antibodies or polypeptides selected in the step c) i) are produced by cells from lymphoid cell lines or lymphoid-derived cell lines or hybridomas or from epithelial kidney cell lines, said antibodies or polypeptides selected in the step c) ii) are produced by cells from non-lymphoid cell lines and said antibodies or polypeptides selected in the step c) iii) are produced by cells from an heterohybridoma fused to cells from an EBV-transformed cell line or to B lymphocytes from human donors.

3. A method according to claim 2, wherein said lymphoid-derived cell lines are rat myeloma cell lines or the hybridoma YB2/0 cell line (ATCC number CRL-1662) or cell lines derived thereof, and/or the epithelial kidney cell line is VERO (ATCC number CCL-81) or cell lines derived thereof, and/or the non-lymphoid cell line is CHO (ATCC number CCL-61) or cell lines derived thereof and/or said heterohybridoma is K6H6B5 (ATCC number CRL-1823) or cell lines derived thereof.

4. A method according to anyone of the preceding claims, wherein the binding assays can be performed using :
i) indicator cells from cell lines that express different Fc receptors on their cell surface,
ii) recombinant Fc receptors comprising FcgammaR ectodomains, Fc receptors derived-peptides.

5. A method according to anyone of the preceding claims, wherein the subset of antibodies or polypeptides selected for their ability to bind to both FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB, and the subset of antibodies or polypeptides selected for their ability to bind to both FcgammaRIIA and FcgammaRIIB are further tested and selected by functional assays for their ability i) to trigger FcgammaRIIIA leading to improved ADCC, increased production of cytokines such as Interleukin-2 (IL-2) and of pro-inflammatory molecules such as Tumor Necrosis Factor alpha (TNF alpha) ; and ii) to trigger FcgammaRIIB, leading to the inhibition of calcium mobilization and to the inhibition of cytokine production such as IL-2 by cells expressing FcgammaRIIB such as B cells and monocytes.

6. A method according to anyone of the preceding claims, wherein said functional assays consist of a calcium mobilization inhibition assay, and/or a cytokine secretion inhibition assay.

7. A method according to claim 5 or 6, wherein the functional assays can further comprise a specific FcgammaRIIIA ADCC assay.

8. Use of cells from lymphoid cell lines or lymphoid-derived cell lines or hybridoma or from epithelial kidney cell lines to produce antibodies that are able to bind to FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB.

9. Use according to claim 8, wherein said antibodies are immunomodulatory antibodies.

10. Use according to claim 8 or 9, wherein said antibodies are both immunomodulatory and cytotoxic antibodies.

11. Use according to anyone of claims 8 to 10, wherein said hybridoma cell line is YB2/0.

12. Use according to anyone of the claims 8 to 10 wherein said epithelial kidney cell line is VERO (ATCC number CCL-81).

13. Use of cells from non-lymphoid cell lines to produce antibodies that do not bind or bind only weakly to FcgammaRIIIA but bind to both FcgammaRIIA and FcgammaIIB.

14. Use according to claim 13, wherein said antibodies are immunomodulatory antibodies.

15. Use according to claim 13 or 14, wherein said antibodies induce ADCC and phagocytosis by monocytes and macrophages expressing FcgammaRIIA.

16. Use according to anyone of claims 13 to 15, wherein said cell from non-lymphoid cell line is CHO (ATCC number CCL-61).

17. Use of cells from an heterohybridoma fused to cells from an EBV-transformed cell line, or to B cells, to produce antibodies that do not bind or bind weakly to both FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB.

18. Use according to claim 17 wherein said antibodies are used as therapeutic alternative to the use of IgG4.

19. Use according to claim 17 or 18, wherein said cells are from the heterohybridoma K6H6B5 (ATCC number CRL-1823) fused to human B cells.

20. An antibody or a polypeptide comprising Fc region of human IgG, characterized in that it contains from 10% to 55% of fucose, from 60% to 98% of galactose.

21. An antibody or a polypeptide according to claim 20, characterized in that it is produced by cells from lymphoid cell lines or lymphoid-derived cell lines or hybridomas or from epithelial kidney cell lines.

22. An antibody or a polypeptide according to claim 21, wherein the hybridoma cell line is the YB2/0 cell line (ATCC number CRL-1662).

23. An antibody or a polypeptide according to claim 21, wherein the epithelial kidney cell line is is VERO (ATCC number CCL-81).

24. An antibody or a polypeptide according to anyone of claims 20 to 23 characterized in that it binds to both FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB.

25. An antibody or a polypeptide according to anyone of claims 20 to 24 characterized in that it is obtainable by the step c) i) of the process according to claims 1 to 7.

26. An antibody or a polypeptide comprising Fc region of human IgG, characterized in that it contains from 70% to 100% of fucose, and from 60% to 98% of galactose.

27. An antibody or a polypeptide according to claim 26, characterized in that it is produced by cells from a non-lymphoid cell line.

28. An antibody or a polypeptide according to claim 27 characterized in that said non-lymphoid cell line is CHO cell line (ATCC number CCL-61).

29. An antibody or a polypeptide according to anyone of claims 26 to 28 characterized in that it binds to both FcgammaRIIA and FcgammaRIIB but does not bind or binds only weakly to FcgammaRIIIA.

30. An antibody or a polypeptide according to anyone of claims 26 to 29 characterized in that it is obtainable by the step c) ii) of the process according to claim 1 to 7.

31. An antibody or a polypeptide comprising Fc region of human IgG, characterized in that it contains from 80% to 100% of fucose, from 60% to 98% of galactose and that contains from 30% to 80% of sialylated forms.

32. An antibody or a polypeptide according to claim 31 characterized in that it is produced by cells from a heterohybridoma fused to EBV-transformed cells or to B lymphocytes from human donors.

33. An antibody or a polypeptide according to claim 32 characterized in that said heterohybridoma is K6H6B5 (ATCC number CRL-1823) fused to cells from an EBV-transformed cell line.

34. An antibody or a polypeptide according to anyone of claims 31 to 33 does not bind or binds only weakly to both FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB.

35. An antibody or a polypeptide according to anyone of claims 31 to 34 characterized in that it is obtainable by the step c) iii) of the process according to claims 1 to 7.

36. An antibody or a polypeptide according to claims 1 to 35 characterized in that it belongs to the IgG1 subclass.

37. An antibody or a polypeptide according to claims 1 to 35 characterized in that it belongs to the IgG3 subclass.

38. A composition comprising at least 80%, preferably at least 95% of antibodies or polypeptides according to one of claims 20 to 25.

39. Use of a composition according to claim 38 to manufacture a medicament for treating cancer, auto-immune diseases, allergies, allo-immunization following transplantation, materno-fœtal allo-immunization, Graft-Versus Host (GVH) reaction or infectious diseases.

40. Use according to claim 39 wherein said cancer is leukemia, lymphoma, myeloma, Sezary syndrome, or solid tumors.

41. Use according to claim 39 wherein said materno-fœtal allo-immunization is the hemolytic disease of the newborn (HDNB).

42. Use according to claim 39 wherein said auto-immune disease is an autoimmune disease involving B cells that produce auto-antibodies such as Systemic Lupus Erythematosis (SLE), Idiopathic Thrombocytopenic Purpura (ITP), Kawasaki syndrome.

43. Use according to claim 39 wherein said allergies are asthma, allergic rhinitis, allergic sinusitis, anaphylactic syndrome, urticaria, angioedema, atopic dermatitis, allergic contact dermatitis and erythema.

44. A composition comprising at least 80%, preferably at least 95% of antibodies or polypeptides according to claims 26 to 30.

45. Use of a composition according to claim 44 for the manufacture of a medicament for treating auto-immune diseases, materno-fœtal allo-immunization, and inflammatory diseases.

46. A composition comprising at least 80%, preferably at least 95% of antibodies or polypeptides according to claims 31 to 35.

47. Use of a composition according to claim 46 for the manufacture of a medicament for treating inflammatory disease, the Crohn disease or the Rheumatoid Arthitis.